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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,996	12/30/1999	JOHANNES CHRISTIANUS VAN GROENINGHEN	49477(1958)	3246
24247	7590	01/31/2006	EXAMINER	
TRASK BRITT P.O. BOX 2550 SALT LAKE CITY, UT 84110			BORGEEST, CHRISTINA M	
			ART UNIT	PAPER NUMBER
			1649	
DATE MAILED: 01/31/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/446,996	<b>Applicant(s)</b> VAN GROENINGHEN, JOHANNES CHRISTIANUS	
	<b>Examiner</b> Christina Borgeest	<b>Art Unit</b> 1649	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-9, 12 and 14-17 is/are pending in the application.
- 4a) Of the above claim(s) 1-9 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>17 August 2005</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Formal Matters***

With regard to the petition to revive the application entered 17 August 2005 was granted on 26 September 2005. The amendment filed 17 August 2005 is acknowledged. Claims 1-9, 12, 14-17 are pending in this application. Claims 1-9 and 12 are withdrawn from consideration as drawn to a non-elected invention. Claims 14-16 have been amended. Claims 14-17 are examined in light of Applicants' species election of GnRH agonists. The text of those sections of Title 34, U.S. Code, not included in this action can be found in a prior office action.

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

### ***Objections Withdrawn – Specification***

The objection to the specification for not capitalizing trademarks is withdrawn in response to Applicants' correction to the specification, filed 17 August 2005.

### ***Objections/Rejections Maintained***

The objection to the specification with regard to compounds described as antagonists in Table 1 are referred to agonists on p. 10, line 3 is maintained. Clarification is required.

***Information Disclosure Statement***

The information disclosure statement filed 17 August 2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because copies of He et al. and Hoitink et al. were not provided. In addition, "Rote Liste" was not considered because no copy was provided and because without any further information, it is not clear what the significance of this citation is. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

***Claim Rejections - 35 USC § 112***

The rejection of claims 14-17 under 35 U.S.C. 112, first paragraph, is maintained. In Applicants' arguments filed 17 August 2005, it is argued that the claims are amended and are now directed to a method for decreasing cellular replication of a tumor originating in one or more of the brain, nervous system or meninges of the brain, Kaposi sarcoma, proliferating glioma, glioblastoma multiforme, medulloblastoma, pinealoma, neuroblastoma, craniopharyngeoma, meningioma, chordoma, Ewing sarcoma or malignant melanoma comprising administering to a subject a therapeutically effective amount of one or more of a GnRH agonist or antagonist. Applicants' indicate in

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arguments that in the case of claim 15, a subject is administered a "TGF- $\beta$  decreasing amount of a GnRH analog." The arguments have been fully considered but are not found persuasive for the following reasons.

As stated in the previous Office action (mailed 22 April 2002), 'Applicant has not provided guidance to indicate that GnRH receptors are present in all of the cancers Applicants' methods are intended to treat. Clinical trial data are not required, but there must be sufficient evidence or guidance to allow one of skill in the art to make and use the invention without undue experimentation. The specification provides only three in vitro experiments indicating that a 15-35% inhibition of proliferation could be obtained in a cell lines using a GnRH agonist, a GnRH antagonist, or LHRH and evidence of varying GnRH receptor levels in some tumor samples. Limited in vitro data such as that provided in the instant application are not predictive of anti-cancer activity. The prior examiner cited Shi et al. (copy provided with previous Office action, mailed 22 April 2002), who report that NCI Anticancer Drug Discovery Program, which uses 60 cell lines, states "the growth inhibitory activity for a single cell line is not very informative" (p. 368). Similarly Johnson et al. (sent out in prior Office action, mailed 22 April 2002) states that preliminary screening of agents in a few specific cell lines generated a large number of candidate agents, and additional screening was required to identify candidates suitable for preclinical development (p. 1424). On the whole, the art teaches that further extensive experimentation is required to test an agent identified by preliminary in vitro screening. Furthermore, Applicants' argument regarding claim 15

does not clarify Applicants' position, as it is not clear what a "TGF- $\beta$  decreasing amount of a GnRH analog" is, since claim 15 recites no such limitation.

In addition, a search performed in STN in medline revealed that the prior art is silent with regard to GnRH agonist treatment of the diseases listed in claims 14-16. The closest link between tumors and GnRH agonist treatment pertained to the treatment of children suffering from cancer with GnRH agonists to delay onset of puberty (Adan et al., Med Pediatr Oncol. 2000; 34:14-19, see abstract). Without sufficient guidance, either in the specification, or the literature, it would require undue experimentation for the skilled artisan to use Applicants' invention.

Finally, the claims encompass all GnRH agonists (as well as antagonists), including those not yet known in the art. The efficacy of any particular compound is dependent upon many variables, including pharmacological and physiological, as well as biochemical factors. Because of the complex nature of all of these factors, it is not predictable which agonists would function as claimed. Due to the large quantity of experimentation necessary to test the many possibilities without such predictability of success would be well outside the realm of routine experimentation, the lack of direction/guidance presented in the specification (as well as the literature) regarding this, the absence of working examples, the complex nature of the invention (refer to Shi et al. and Johnson et al.), and the breadth of the claims which fail to recite limitations upon what GnRH agonists (or antagonists) can be used in treatment, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 10, 12 and 13-18 of copending Application No. 10/327,621. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '621 Application are drawn to a "method for decreasing cellular replication of GnRH-positive oat cell carcinoma, malignant melanoma, Kaposi sarcoma or proliferating glioma comprising administering to a cell a replication decreasing amount of a GnRH agonist selected from the group consisting of luteinizing hormone releasing hormone, leuprorelin, triptorelin, buserelin, goserelin and pharmacologically acceptable salts

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thereof", and another cytotoxic agent, and the instant claims are drawn to a "method for decreasing cellular replication of a tumor originating in one or more of the brain, nervous system or meninges of the brain, wherein the illness is selected from group consisting of Kaposi sarcoma, proliferating glioma, glioblastoma multiforme, medulloblastoma, pinealoma, neuroblastoma, craniopharyngeoma, meningioma, chordoma, Ewing sarcoma or malignant melanoma comprising administering to a subject a therapeutically effective amount of one or more of a GnRH agonist or GnRH antagonist. The broad claim language in the instant application is encompassed by claims 9, 10, 12 and 13-18 of copending Application No. 10/327,621.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

No claim is allowed.

This is a continuing examination of Application No. 09/446,996. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christina Borgeest, Ph.D.

*Elizabeth C. Kemmerer*

ELIZABETH KEMMERER  
PRIMARY EXAMINER